

Assessment of 25(OH)D vitamin concentration in plasma of residents of Lodz with metabolic syndrome in pre- and postmenopausal period

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Abstract

Introduction: Vitamin D deficiency is a risk factor for metabolic syndrome disorders and the occurrence of these disorders greatly contributes to the deficiency of vitamin D. Postmenopausal women are particularly prone to that deficiency.

Aim: The aim of the study was to assess vitamin D concentration in the plasma of pre- and postmenopausal women, with or without metabolic syndrome.

Material and methods: The study included 141 women aged 26-77 (the mean age 58.74 years old), divided into 4 groups depending on the pre- or postmenopausal period and diagnosed or not with metabolic syndrome according to the International Diabetes Federation criteria (2005). Vitamin D concentration was assessed by LIAISON[®] test using chemiluminescent immunoassay (CLIA) technology.

Results: The mean vitamin D concentration was the highest among premenopausal women without metabolic syndrome (24.32 ng/ml), it was insignificantly higher than in postmenopausal women without metabolic syndrome (23.52 ng/ml) and significantly higher than in both groups with metabolic syndrome – premenopausal (19.86 ng/ml) and postmenopausal women (9.32 ng/ml). The recommended plasma 25(OH)D concentration was not found in any of postmenopausal women with diagnosed metabolic syndrome.

Conclusions: Postmenopausal women with metabolic syndrome had a significantly lower 25(OH)D vitamin concentration in plasma than postmenopausal women without metabolic syndrome. The frequency of vitamin D deficiency in women with metabolic syndrome was very high, significantly higher than in women without metabolic syndrome.

Key words: metabolic syndrome, menopause, vitamin D.

Introduction

Cardiovascular diseases have been the main cause of mortality in Poland for many years, including premature death and the incidence is systematically growing. These diseases contribute to an increase in the number of disabled people and the cost of medical care. The problem of the so-called metabolic syndrome (MS), which includes metabolic risks of atherosclerosis, has been known to doctors for a long time. Results of studies which have been conducted for some years confirm that vitamin D deficiency is a risk factor for MS disorders, including obesity, arterial hypertension, diabetes. On the other hand, there are justified assumptions that these disorders greatly contribute to the deficiency of

vitamin D [1-3]. Vitamin D is provided to the body *per os* and is generated in the skin by ultraviolet radiation B (UVB) [4-6]. Some European population studies demonstrated very low levels of 25-hydroxyvitamin D – 25(OH)D – in the plasma, which confirms an insufficient level of vitamin D in a population, particularly in winter season. Patients with MS are particularly prone to the deficit of vitamin D. In their plasma, the level of 25(OH)D is lower than in healthy people. This also applies to postmenopausal women, in whom a low level of vitamin D significantly contributes to an increase in the risk of osteoporosis and bone fractures [7-9].

The aim of the study was to assess vitamin D concentration in the plasma of pre- and postmenopausal women, with or without MS.

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Material and methods

The study included 141 women from Lodz aged 26-77 (the mean age 58.74 years old), divided into following groups:

- group I (control): 24 women before menopause, without MS, aged 26-49 (the mean age 37.83 years old),
- group II (control): 36 women after menopause, without MS, aged 50-65 (the mean age 55.42 years old),
- group III: 30 women before menopause, with MS, aged 38-45 (the mean age 41.95 years old),
- group IV: 51 women after menopause, with MS, aged 56-77 (the mean age 65.52 years old).

General characteristics of study participants are shown in Table I.

The division criteria was the last menstruation which happened at least 12 months before the inclusion in the study. Moreover, the respondents were diagnosed with MS on the basis of the International Diabetes Federation (IDF) criteria. The syndrome included central obesity (waist circumference > 80 cm) and at least two more factors: triglyceride concentration ≥ 1.7 mmol/l, HDL cholesterol level < 1.3 mmol/l, fasting glucose level ≥ 6.1 mmol/l, arterial pressure $\geq 130/85$ mmHg. All the studied women were residents of Lodz, non-smokers and did not take vitamin supplements in the last year. The study was conducted between January 2012 and April 2013 in the Department of Internal Medicine and Nephrodiabetology, Medical University of Lodz.

Blood for laboratory tests was taken from the basilica vein. The blood samples were used to assess the concentration of 25(OH)D with the application of the LIAISON[®] test using chemiluminescent immunoassay (CLIA) technology. The plasma level of 25(OH)D above 30 ng/ml was considered normal, between 20 ng/ml

and 30 ng/ml – suboptimal (hypovitaminosis) and below 20 ng/ml – insufficient (deficiency).

Program Statistica 7.1 PL and Office 2010 were used for statistical purposes. The normal distribution was computed with the Shapiro-Wilk test. If the distribution of at least one variable was different from the normal one, the authors applied the Mann-Whitney's test. In the case of variables with nominal scales, the authors computed the rate of occurrence of the particular feature. For comparative purposes the authors used the χ^2 test with Yates' correction. The authors adopted the significance level $p < 0.05$.

The Bioethics Committee of Medical University of Lodz gave its consent to such a study to be performed (No. RNN/556/10/KB). All the respondents gave their written consent to be included in the study.

Results

The range of 25(OH)D levels in the plasma of women without MS ranged from 11.55 to 53.36 ng/ml in patients before menopause and from 13.39 to 45.87 ng/ml in patients after menopause. In the group of patients with diagnosed MS the levels ranged from 14 to 31 ng/ml in the group of patients before menopause and 4-17.3 ng/ml in patients after menopause.

The highest mean concentration of vitamin D was observed in females without MS and before menopause (24.34 ± 8.84 ng/ml) and it was insignificantly higher than the mean concentration of vitamin D in postmenopausal women without MS (23.52 ± 6.84 ng/ml) and significantly higher than in the two remaining groups with diagnosed MS.

The lowest 25(OH)D level was noted in postmenopausal women with diagnosed MS (9.32 ± 3.58 ng/ml).

Tab. I. General characteristics of study participants

Parameters	Group I	Group II	Group III	Group IV
	Mean \pm SD	Mean \pm SD	Mean \pm SD	Mean \pm SD
Age (years)	37.83 \pm 2.6	55.42 \pm 3.5	41.95 \pm 4.6	65.52 \pm 5.2
BMI (kg/m ²)	23.42 \pm 2.51	27.26 \pm 4.22	29.68 \pm 4.28	34.26 \pm 5.18
Waist (cm)	79.5 \pm 2.6	87.1 \pm 3.5	95.6 \pm 8.9	110.6 \pm 13.3
Systolic BP (mmHg)	114.9 \pm 7.9	125.8 \pm 5.6	148.5 \pm 7.2	147.7 \pm 15.6
Diastolic BP (mmHg)	80.7 \pm 4.3	89.5 \pm 10.5	90.8 \pm 5.5	98.4 \pm 10.6
HDL-cholesterol (mmol/l)	0.98 \pm 0.27	1.05 \pm 0.43	1.07 \pm 0.15	1.15 \pm 0.32
LDL-cholesterol (mmol/l)	3.31 \pm 0.49	3.67 \pm 0.56	3.49 \pm 1.78	3.87 \pm 1.14
Triglycerides (mmol/l)	1.69 \pm 1.1	1.89 \pm 1.02	2.26 \pm 1.06	2.91 \pm 0.88
Total cholesterol (mmol/l)	4.91 \pm 1.45	5.32 \pm 0.89	5.67 \pm 1.24	4.78 \pm 1.22
Glucose (mmol/l)	5.17 \pm 0.95	5.21 \pm 0.96	7.01 \pm 0.99	8.08 \pm 3.69

SD – standard deviation, BMI – body mass index, BP – blood pressure, HDL – high-density lipoprotein, LDL – low-density lipoprotein

A significantly higher concentration of vitamin D in patients with diagnosed MS was observed in females before menopause rather than after menopause (19.86 ± 4.78 ng/ml and 9.32 ± 3.58 ng/ml, respectively, $p < 0.001$) (Table II).

The highest fraction of patients with the recommended 25(OH)D concentration in the plasma was observed in females without diagnosed MS before menopause (0.21) significantly more often than in the other groups. In this group every second patient (0.54) was diagnosed with hypovitaminosis and every fourth one (0.25) – vitamin D deficiency.

With regard to women in the post-menopausal period without MS, the recommended 25(OH)D concentration in the plasma was observed in 0.17, hypovitaminosis – in 0.47 and vitamin deficiency – in 0.36.

In the group of women in the pre-menopausal period with MS, the recommended 25(OH)D concentration was observed only in 0.07 of patients, in 0.4 the authors observed hypovitaminosis and in 0.53 – vitamin D deficiency.

With regard to women with MS after menopause, no woman had the recommended 25(OH)D concentration or even hypovitaminosis (Table III).

Discussion

Vitamin D deficiency, which has been mainly considered a risk factor for rickets and osteoporosis, also increases the risk of development of metabolic disorders such as diabetes, arterial hypertension, autoimmune disturbances, and cardiovascular and neoplastic diseases. Pleiotropic activity of vitamin D was observed in

molecules, cells, tissues and organs and the vitamin D receptor was already identified in dozens of places in the human body. Thus, meeting demands for vitamin D, diagnosing its deficiency and determining guidelines on supplementation are important steps in management procedures for metabolic syndrome. Females in the post-menopausal period are particularly prone to an increased risk of vitamin D deficiency and its health consequences.

In the conducted study the authors observed a significantly lower level of vitamin D in the plasma of patients with diagnosed metabolic syndrome in comparison to patients without the syndrome, both in the pre- and post-menopausal period. In the group without metabolic syndrome, the 25(OH)D concentration observed in women in the pre- and post-menopausal period was not significantly different.

In a study conducted by Napiórkowska *et al.* on 274 elderly females, randomly selected from a general population, the mean concentration of vitamin D was 13.6 ng/ml [10]. Skalska *et al.* examined 46 women aged 61-95 years old, in whom the mean 25(OH)D concentration was 15.2 ± 9.1 ng/ml [11]. Multicentre studies conducted on 8532 females in the post-menopausal period (the mean age 74.2 years old) in a few European countries showed that the mean 25(OH)D concentration was 24.4 ng/ml. The lowest level of vitamin D was observed in France (25.75 ng/ml) and the highest in Spain (34 ng/ml) [12]. Arunbah *et al.* conducted a study on 410 healthy women aged 20-80 years old. The results demonstrated that the mean 25(OH)D concentration was 21.7 ± 13.8 ng/ml and it decreased with an increase in the amount of fat tissue [13].

Tab. II. Concentration of 25(OH)D vitamin in plasma (ng/ml)

	Group I	Group II	Group III	Group IV
Range of assessed concentration	11.55-53.36	13.39-45.87	14-31	4-17.3
Arithmetic mean	24.34	23.52	19.86	9.32
Standard deviation	8.84	6.84	4.78	3.58
Median	23.43	22.64	19.565	8.9

Test $Z^{II,III}$ Mann-Whitney = 4.81, $p > 0.05$, Test $Z^{I,III}$ Mann-Whitney = 5.51, $p < 0.001$, Test $Z^{I,IV}$ Mann-Whitney = 7.54, $p < 0.001$
 Test $Z^{II,III,IV}$ Mann-Whitney = 6.52, $p < 0.001$, Test $Z^{I,II,IV}$ Mann-Whitney = 7.33, $p < 0.001$, Test $Z^{III,IV}$ Mann-Whitney = 7.57, $p < 0.001$

Tab. III. Structure of 25(OH)D vitamin concentration in plasma (ng/ml)

	Group I	Group II	Group III	Group IV
	Fraction (n)	Fraction (n)	Fraction (n)	Fraction (n)
0-20 (deficiency)	0.25 (6)	0.36 (13)	0.53 (16)	1 (51)
21-30 (hypovitaminosis)	0.54 (13)	0.47 (17)	0.4 (12)	–
31-80 (recommended level)	0.21 (5)	0.17 (6)	0.07 (2)	–

$\chi^2_{I,II} = 11.17$, $C = 0.396$, $p < 0.01$, $\chi^2_{I,III} = 12.15$, $C = 0.429$, $p < 0.01$, $\chi^2_{I,IV} = 1.81$, $C = 0.154$, $p < 0.01$
 $\chi^2_{II,III} = 7.32$, $C = 0.316$, $p < 0.01$, $\chi^2_{II,IV} = 3.39$, $C = 0.194$, $p < 0.01$, $\chi^2_{III,IV} = 1.083$, $C = 0.115$, $p < 0.01$

According to the Third National Health and Nutrition Examination Survey (NHANES), conducted on a representative group of the American population, the mean 25(OH)D concentration in patients with metabolic syndrome was 26.8 ng/ml. The 25(OH)D level was statistically lower in patients with diagnosed metabolic syndrome in comparison to the mean level in patients without the syndrome [14]. Botella-Carretero *et al.* conducted a study on patients with morbid obesity and observed significantly lower levels of vitamin D in the group with metabolic syndrome, whereas such observations were not made in the group without metabolic syndrome [15]. Cigolini *et al.* conducted a study on patients with type 2 diabetes and noted the mean level of vitamin D of 19.7 ± 10 ng/ml. The level was significantly lower in comparison to patients without diagnosed type 2 diabetes [16]. Wortsman *et al.* in their study observed that the mean 25(OH)D concentration in obese patients was 20.0 ± 3.4 ng/ml and it was significantly lower in comparison to patients with normal body weight [17].

Many studies conducted on populations confirm a common deficiency of vitamin D in healthy people. There is a relationship between this deficiency and cardiovascular diseases so it is not surprising that a low concentration of vitamin D in the plasma of patients with metabolic syndrome is very common [18-21]. In their own study the authors observed a deficiency of vitamin D in 0.25 of women in the pre-menopausal period and in 0.36 of women in the post-menopausal period without metabolic syndrome. In the group of females with diagnosed metabolic syndrome, 0.53 of pre-menopausal and all post-menopausal women demonstrated a deficiency of 25(OH)D in the plasma. With regard to patients with metabolic syndrome, only 0.07 of pre-menopausal women demonstrated the recommended vitamin D concentration in the plasma. The recommended 25(OH)D concentration was observed significantly more often in women in the pre-menopausal period rather than in the post-menopausal period and also in women without metabolic syndrome rather than in women with such syndrome. Many studies confirm that the deficiency of 25(OH)D is more frequently found in patients with metabolic syndrome or its some components. Botella-Carretero *et al.* observed that the frequency of deficiency of vitamin D was significantly higher in obese patients with metabolic syndrome than in obese patients without metabolic syndrome (60.9% vs. 33.3%, respectively) [15]. Similar observations were made in a study conducted by Ford *et al.* [14]. Lee *et al.* evaluated a relationship between deficiency of vitamin D and occurrence of myocardial infarction. In this study in only 4% of patients the recommended 25(OH)D concentration in the plasma was observed. Seventy-five percent of patients demonstrated a deficiency of vitamin D and another 21% – hypovitaminosis [22]. Anderson *et al.* assessed the effect of vitamin D on the development of cardiovascular

diseases after analyzing the database of 41 504 outpatients, aged 21-55 years old, where the majority were females (74.8%). They observed a normal level of 25(OH)D in the plasma of 36% of the patients; in 47%, the level was decreased (16-36 ng/ml) and in 17%, the authors observed a deficiency of vitamin D (< 15 ng/ml) [23].

Polish data on deficiency of vitamin D are incomplete. According to data gathered in the OPTIFORD project, conducted in five European countries (including Poland), 90% of women demonstrate a deficiency of 25(OH)D in the plasma [10]. A study conducted in a few European countries (including Poland) confirmed that 79.6% of post-menopausal patients demonstrated a deficiency of vitamin D [10]. Napiórkowska *et al.* analyzed a population of elderly women and noted a vitamin D deficiency in 83.2% of them [10]. Skalska *et al.* observed an abnormal concentration of 25(OH)D in 87.1% of elderly patients (the mean age 79.62 ± 7.4 years old), of whom the majority were females [11]. Bhattoa *et al.* examined post-menopausal women from Hungary and observed different levels of a vitamin D deficiency at different times of a year 46.3-71% [24]. Hill *et al.* conducted a study on 76 post-menopausal women and observed a low level of 25(OH)D in the plasma all year round [25]. Lips *et al.* noted a deficiency of vitamin D in 57.9% of post-menopausal women [26]. Pfeifer *et al.* observed in their study a too low level of vitamin D in 91% of women in the post-menopausal period [27]. Kuchuk *et al.* evaluated the frequency of insufficient levels of vitamin D in post-menopausal women, affected by osteoporosis. In this group, the level of 25(OH)D below 20 ng/ml was observed in 73.5% of women [28]. Andersen *et al.* assessed the level of vitamin D in teenagers and elderly women from the north of Europe (Denmark, Finland, Ireland and Poland). The study group included 199 teenagers (the mean age 12.6 years old) and 221 women (the mean age 71.8 years old). Deficiency of vitamin D was observed in 92% of the studied elderly women and 37% of the teenage girls [29]. Lucas *et al.* analyzed a group of 1606 post-menopausal women, inhabitants of warm, sunny countries. They observed sub-optimal concentrations of 25(OH)D in 58-74% of the respondents [30].

Conclusions

Post-menopausal women with diagnosed MS demonstrated significantly lower plasma concentrations of 25(OH)D than post-menopausal women not affected by that syndrome.

In the group of women without MS, the mean concentration of 25(OH)D was not significantly different in the pre- and post-menopausal periods.

The occurrence of vitamin D deficiency in the group of women with MS was very high, significantly higher in comparison with women without MS.

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Disclosure

Authors report no conflicts of interest.

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